

REMARKS

Claims 5 and 8-12 are pending in the application, with claims 5 and 8 being the independent claims. Claims 1-4, 6 and 7 were cancelled by previous amendment without prejudice to or disclaimer of the subject matter therein.

No amendments are being made to the pending claims in the present Reply. The listing of claims above is being provided solely for the convenience of the Examiner.

Applicant respectfully requests reconsideration of this application in view of the comments that follow.

I. Rejection Under 35 USC § 103

The Examiner rejects claims 5 and 8-12 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ahrén *et al.*, *Eur. J. Pharmacol.* 404:239-245 (2000) ("Ahrén 2000") in view of Nauck *et al.*, *Diabetes Care* 21:1925-1931 (1998) ("Nauck"). (Office Action, at page 2, lines 19-21.) Applicant respectfully traverses this rejection.

Specifically, the Examiner contends that Nauck teaches that a similar glucose threshold for GLP-1-induced insulin secretion is still active in patients with true sulfonylurea secondary failure, and that, as a consequence, one of ordinary skill in the art would have a reasonable expectation that treating a diabetic patient with secondary sulfonylurea failure with a DPP-IV inhibitor would be successful at preserving endogenous GLP-1 levels, which results in stimulation of insulin secretion in the patients. (Office Action, at page 3, lines 6-12.)

Applicant respectfully reiterates the arguments presented in the previous Amendment and Reply filed on March 31, 2008. In particular, Applicant submits that Nauck does not teach that endogenous levels of GLP-1 increase in response to inhibition of DPP-IV in a diabetic patient with sulfonylurea secondary failure, or that any increase in endogenous GLP-1 in such patients, if it did occur, would be effective in lowering plasma glucose levels of the diabetic patient with sulfonylurea secondary failure.

Thus, there would have been no reason for one of skill in the art, in view of Ahrén 2000 and Nauck, to arrive at Applicant's claimed methods of treating diabetes with

sulfonylurea secondary failure or of promoting insulin secretion in a diabetic patient with sulfonylurea secondary failure. Accordingly, the methods as currently claimed would not have been obvious in light of Ahrén 2000 and Nauck.

Applicant also provides the following additional comments concerning the advantages of the claimed method.

Administration of a DPP-IV inhibitor, as in Applicant's claimed method, is very advantageous from the viewpoint of the objective of the claimed invention, *i.e.*, treatment of diabetes with sulfonylurea (SU) secondary failure as compared with a GLP-1 analogue. This is because administration of a DPP-IV inhibitor can be used safely with minimal side effects, as opposed to administration of a GLP-1 analogue. See Applicant's specification, as originally filed, *e.g.*, at page 4, lines 8-14.

See also the attached article, Amori *et al.*, *JAMA* 298:194-206 (2007) ("Amori"), which discloses a comparison of the side effects of GLP-1 analogues and DPP-IV (DPP4) inhibitors. On page 203, Table 3, of Amori, side effects of GLP-1 analogues and DPP-IV inhibitors are compared. When risk ratios are compared with each other (the higher the risk ratio is, the more severe the side effect), risks of hypoglycemia, nausea, vomiting, etc. of GLP-1 analogues are higher than for DPP-IV inhibitors. While a DPP-IV inhibitor has a risk such as infection (see page 202, the paragraph beginning from line 11 of the left-hand column, etc.), no hypoglycemia is reported with respect to a DPP-IV inhibitor (see page 201, the last paragraph in the right-hand column, the last paragraph). On the other hand, hypoglycemia is reported when a GLP-1 analogue is combined with a SU drug (see page 201, the paragraph beginning from line 23 of the left-hand column). Since hypoglycemia is the most noteworthy side effect for treatment of diabetes, as mentioned above, a DPP-IV inhibitor is much advantageous.

Applicant believes that the rejection of claims 5 and 8-12 under 35 U.S.C. § 103 has been overcome. Accordingly, Applicant respectfully requests that the Examiner withdraw this rejection.

CONCLUSION

Based on the foregoing remarks, Applicant respectfully requests that the Examiner reconsider all rejections and that they be withdrawn. Applicant believes that the present

application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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